

PATENT COOPERATION TREATY

PCT/US99/17366

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 07 April 2000 (07.04.00)	Applicant's or agent's file reference 0152.00345
International application No. PCT/US99/17366	Priority date (day/month/year) 30 July 1998 (30.07.98)
International filing date (day/month/year) 30 July 1999 (30.07.99)	
Applicant ZUCKERMAN, Kenneth, S. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
17 February 2000 (17.02.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Olivia RANAIVOJAONA
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

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WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 : C12N	A2	(11) International Publication Number: WO 00/06696	(43) International Publication Date: 10 February 2000 (10.02.00)
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(21) International Application Number: PCT/US99/17366
(22) International Filing Date: 30 July 1999 (30.07.99)
(30) Priority Data:
60/094,695 30 July 1998 (30.07.98) US

(71) Applicant (for all designated States except US): UNIVERSITY OF SOUTH FLORIDA [US/US]; 4202 Fowler Avenue - FAO 126, Tampa, FL 33620-7900 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ZUCKERMAN, Kenneth, S. [US/US]; 15610 Cochester Drive, Tampa, FL 33647 (US). LIU, Richard, Y. [US/US]; 18403 Canary Lane, Lutz, FL 33549 (US).

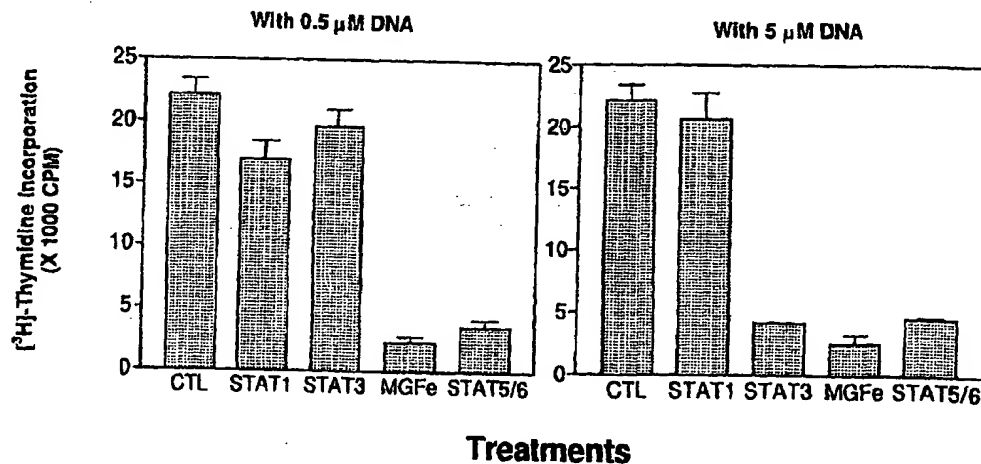
(74) Agents: KOHN, Kenneth, I. et al.; Kohn & Associates, Suite 410, 30500 Northwestern Highway, Farmington Hills, MI 48334 (US).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published

Without international search report and to be republished upon receipt of that report.

(54) Title: METHOD FOR THE MODULATION OF FUNCTION OF TRANSCRIPTION FACTORS



(57) Abstract

There is provided a method of modulating the function of transcription factor by administering an effective amount of an oligonucleotide containing optimal nucleotide binding sites for the transcription factor. A therapeutic agent having an effective amount of an oligonucleotide for modulating function of transcription factors and a pharmaceutically acceptable carrier is also provided. Also provided is a treatment of patients having illnesses in which the activation of transcription factors play a role by administering to a patient an effective amount of an oligonucleotide which competitively binds the related transcription factor.

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Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6:

A61K 31/70, C07H 21/00**A3**

(11) International Publication Number:

WO 00/06696

(43) International Publication Date:

10 February 2000 (10.02.00)

(21) International Application Number: PCT/US99/17366

(22) International Filing Date: 30 July 1999 (30.07.99)

(30) Priority Data:

60/094,695

30 July 1998 (30.07.98)

US

(71) Applicant (for all designated States except US): UNIVERSITY OF SOUTH FLORIDA [US/US]; 4202 Fowler Avenue - FAO 126, Tampa, FL 33620-7900 (US).

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(75) Inventors/Applicants (for US only): ZUCKERMAN, Kenneth, S. [US/US]; 15610 Cochester Drive, Tampa, FL 33647 (US). LIU, Richard, Y. [US/US]; 18403 Canary Lane, Lutz, FL 33549 (US).

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Published*With international search report.**Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.*

(88) Date of publication of the international search report:

16 March 2000 (16.03.00)

(54) Title: METHOD FOR THE MODULATION OF FUNCTION OF TRANSCRIPTION FACTORS

(57) Abstract

There is provided a method of modulating the function of transcription factor by administering an effective amount of an oligonucleotide containing optimal nucleotide binding sites for the transcription factor. A therapeutic agent having an effective amount of an oligonucleotide for modulating function of transcription factors and a pharmaceutically acceptable carrier is also provided. Also provided is a treatment of patients having illnesses in which the activation of transcription factors play a role by administering to a patient an effective amount of an oligonucleotide which competitively binds the related transcription factor.

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DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17366

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 31/70; C07H 21/00

US CL : 514/44; 536/24.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/375; 514/44; 536/23.1, 24.1, 24.5 ..

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Extra Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,683,985 A (CHU et al.) 04 November 1997, see entire document.	1, 2, 5-12, 16-19 ----- 3, 4, 13, 14
X	WO 96/35430 A1 (FUJISAWA PHARMACEUTICAL CO., LTD.) 14 November 1996, see abstract.	1, 2, 4-11, 16-19
X	SHARAMA et al. The NF-kB Transcription Factor in Oncogenesis. Anticancer Research, April 1996, Vol. 16, pages 589-596, especially page 591, 2nd full paragraph and paragraph bridging pages 259 and 260.	4
Y	US 5,712,094 A (SEIDEL et al.) 27 January 1998, see entire document, especially column 10, lines 30-51.	3, 13, 14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*A* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

15 DECEMBER 1999

Date of mailing of the international search report

27 JAN 2000

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
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Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

THOMAS G. LARSON, PH.D.

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/17366

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

WEST (USPT, DWPI, JPAB, EPAB); STN (BIOSIS, CAPLUS, LIFESCI, MEDLINE, REGISTRY), GENBANK EMBL
Search Terms: decoy, oligonucleotide, transcription factor, NF-kB, STAT, STAT5, cancer leukemia, malignant.

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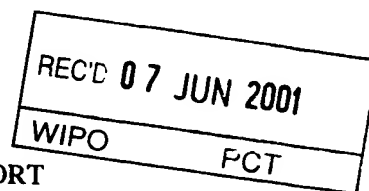
14

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference 0152.00345		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US99/17366	International filing date (day/month/year) 30 July 1999 (30.07.1999)	Priority date (day/month/year) 30 July 1998 (30.07.1998)	
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/70; C07H 21/00 and US Cl.: 514/44; 536/24.5			
Applicant UNIVERSITY OF SOUTH FLORIDA			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
These annexes consist of a total of 3 sheets.

3. This report contains indications relating to the following items:
 - I ☒ Basis of the report
 - II ☐ Priority
 - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
 - IV ☐ Lack of unity of invention
 - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - VI ☐ Certain documents cited
 - VII ☐ Certain defects in the international application
 - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Thomas G. Larson, Ph.D. Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/17366

I. Basis of the report

1. With regard to the elements of the international application:*

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-32 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the claims:
pages 33-35, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the drawings:
pages 1-6, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____
- ☒ the sequence listing part of the description:
pages None, as originally filed
pages NONE, filed with the demand
pages 1-3, filed with the letter of 19 October 1999

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item. These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages None
- ☒ the claims, Nos. None
- ☒ the drawings, sheets/fig. None

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/17366

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims <u>3 and 13-15</u>	YES
	Claims <u>1, 2, 4-12, and 16-19</u>	NO
Inventive Step (IS)	Claims <u>15</u>	YES
	Claims <u>1-14 and 16-19</u>	NO
Industrial Applicability (IA)	Claims <u>1-19</u>	YES
	Claims <u>NONE</u>	NO

2. CITATIONS AND EXPLANATIONS (Rule 70.7)

Please See Continuation Sheet

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/17366

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

useful to have inhibitors of the STAT family of transcription factors to treat conditions stemming from cytokine-induced disease states. One would have had a reasonable expectation of success because Seidel et al. provide oligonucleotides that bind STAT transcription factors that provide the required binding sequence to use as oligonucleotide decoys as taught by Chu et al.

Claim 15 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest oligonucleotide decoys having the sequences set forth in SEQ. ID. NOS: 1-3.

Claims 1-19 meet the criteria set out under PCT Article 33(4).

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

V. 2. Citations and Explanations:

Claims 1, 2, 5-12, and 16-19 lack novelty under PCT Article 33(2) as being anticipated by Chu et al. (US Patent No. 5,683,985).

Chu et al. teach oligonucleotide decoys comprising a binding site for a transcription factor (col. 2, lns. 1-27). Chu et al. further teach methods for modulating the function of a transcription factor by providing such an oligonucleotide to a subject (col. 2, lns. 28-34). Chu et al. teach the therapeutic application of the decoys in the treatment of various disease states, including cancer, and the administration of the decoys in compositions comprising pharmaceutically acceptable carriers (col. 4, lns. 36-60).

Claims 1, 2, 4-11, and 16-19 lack novelty under PCT Article 33(2) as being anticipated by WO 96/35430.

The WO 96/35430 teaches the administration of composition comprising a decoy oligonucleotide having an NF-kB binding site to treat diseases caused by NF-kB expression including metastatic cancer.

Claims 1, 2, 4, 7-11, and 19 lack novelty under PCT Article 33(2) as being anticipated by Sharma et al.

Sharma et al. disclose the inhibition of NF-kB and relA transcription factors in cells in vitro, and the inhibition of tumor cell growth in vitro using transcription factor decoys comprising binding sites for these transcription factors (p. 591, col. 2, 1st full paragraph to paragraph bridging pp. 591-592).

Claims 1-14 and 16-19 lack an inventive step under PCT Article 33(3) as being obvious over Chu et al. (US Patent No. 5,683,985) in view of Seidel et al. (US Patent No. 5,712,094).

Chu et al. teach generic oligonucleotide decoys comprising a binding site for a generic transcription factor (col. 2, lns. 1-27, Figs. 1-3). Chu et al. further teach methods for modulating the function of a transcription factor by providing such an oligonucleotide decoy comprising the binding site for the transcription factor to a subject (col. 2, lns. 28-34). Chu et al. teach the therapeutic application of the decoys in the treatment of various disease states, including cancer, and the administration of the decoys in compositions comprising pharmaceutically acceptable carriers (col. 4, lns. 36-60). Chu teaches a large number of transcription factor binding sites and treatment of conditions from expression of these factors (col. 2, 57-col. 4, ln. 35).

Seidel et al. teaches oligonucleotides that bind STAT family transcription factors (col. 10, lns. 10-63). Seidel et al. provide examples of oligonucleotides comprising such sequences binding STAT transcription factors (col. 17, lns. 21-67, Tables 1 and 2, Figs. 1A and 1B). Seidel et al. teach the STAT 5 consensus binding sequence TTCNNNGAA (col. 10, ln. 39) and the sequence TTCCCGGAA (SEQ. ID. NO: 11, col. 10, ln. 49). Seidel et al. teach a large number of cytokines that activate STAT-mediated transcription (col. 11, lns. 25-45) and that it would be useful to have inhibitors of STAT-mediated gene transcription to use a pharmaceutical agents in for the intervention in cytokine-induced disease states and conditions (col. 14, lns. 14-17).

It would have been obvious to combine the method of using oligonucleotide decoys to inhibit transcription factors of Chu et al. with the STAT family binding oligonucleotides of Seidel et al. to inhibit STAT family transcription factors. One would have been motivated to do so because Chu et al. specifically teach the decoy-mediated inhibition of the activity of a transcription factor as a means for the treatment of a condition stemming from the activity of the transcription factor while Seidel et al. teach that it would be

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US99/17366

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of Certain Documents Cited

1. Certain published documents (Rule 70.10)

Application No

Publication Date

Filing Date

Priority date (valid claim)

Patent No.

(day/month/year)

(day/month/year)

(day/month/year)

None

None

None

None

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure

Date of non-written disclosure

Date of written disclosure referring to
non-written disclosure

(day/month/year)

(day/month/year)

None

None

None

INTERNATIONAL SEARCH REPORT

International application No.
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A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 31/70; C07H 21/00

US CL : 514/44; 536/24.5

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/375; 514/44; 536/23.1, 24.1, 24.5

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ^a	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 5,683,985 A (CHU et al.) 04 November 1997, see entire document.	1, 2, 5-12, 16-19 ----- 3, 4, 13, 14
X	WO 96/35430 A1 (FUJISAWA PHARMACEUTICAL CO., LTD.) 14 November 1996, see abstract.	1, 2, 4-11, 16-19
X	SHARAMA et al. The NF-kB Transcription Factor in Oncogenesis. Anticancer Research, April 1996, Vol. 16, pages 589-596, especially page 591, 2nd full paragraph and paragraph bridging pages 259 and 260.	4
Y	US 5,712,094 A (SEIDEL et al.) 27 January 1998, see entire document, especially column 10, lines 30-51.	3, 13, 14



Further documents are listed in the continuation of Box C.



See patent family annex.

^a Special categories of cited documents:^A document defining the general state of the art which is not considered to be of particular relevance^E earlier document published on or after the international filing date^L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)^O document referring to an oral disclosure, use, exhibition or other means^P document published prior to the international filing date but later than the priority date claimed^T

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

^X

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

^Y

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

^Z

document member of the same patent family

Date of the actual completion of the international search

15 DECEMBER 1999

Date of mailing of the international search report

27 JAN 2000

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